UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trad mark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/340,196	06/28/99	KATO	R 990701

023850 HM12/0706
ARMSTRONG,WESTERMAN, HATTORI,
MCLELAND & NAUGHTON, LLP
1725 K STREET, NW, SUITE 1000
WASHINGTON DC 20006

EXAMINER	
HUNT, J	
ART UNIT	PAPER NUMBER
1642	15

DATE MAILED: 07/06/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/340,196	Kato et al.
Examiner	**Art Unit**
Jennifer Hunt	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *12/15/2000, and 4/16/2001*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *49-77* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *49-77* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Continued Prosecution Application

1. The request filed on 12/15/2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/340,196 is acceptable and a CPA has been established. An action on the CPA follows.

2. Acknowledgment is made of applicant's cancellation of all previously pending claims, and subsequent addition of new claims 49-77. Claims 49-77 are pending in the application and under consideration.

Claim Rejections - 35 U.S.C. § 112

3. Claims 49-77 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of detecting sugar chain variations in thyroglobulin molecules, does not reasonably provide enablement for methods of differentiating any of "two types" of thyroglobulins' and methods of diagnosing cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the

prior art, 6) the relative skill of those in the art, 7) the predictability of the unpredictability of the art, and 8) the breadth of the claims (see Ex parte Forman, 230 USPQ 546, BPAI, 1986).

The claims are broadly drawn to methods of detecting "one of two types" of thyroglobulins, using an antibody which binds to both types of thyroglobulins and an antibody or lectin which binds to only one of the two types.

The specification discloses a specific method in which a constant region, common to human thyroglobulins is bound by an antibody and subsequently a lectin which binds to a sugar chain is used to determine thyroglobulin sugar chain variants which correspond to malignancies.

The claims broadly encompass differentiating any number of different types of thyroglobulin by binding to a sugar chain molecule, however sorting thyroglobulins by sugar chain variations would not differentiate any "type" of thyroglobulin, by rather only those that have a detectable difference in their sugar chain structure. Any "type" of thyroglobulin could refer to other non-sugar chain modifications, sequence variations, or even production in distinct species, etc. Detection of sugar chain molecule variations would not be indicative of the broadly claimed "types" of thyroglobulins.

Additionally, with regard to the claims which recite diagnosis of a malignancy, use of specific lectins which are known to bind to sugar chain modifications in the thyroglobulins of cancer patients would be required to diagnose cancer. The claims broadly recite any antibody or lectin, regardless of what it binds, many of which would in no way correlate to malignancy and thus would not function unless the appropriate lectins were used.

Thus the disclosure of one art known method of detecting thyroglobulin sugar chain variants is insufficient support under the first paragraph of 35 U.S.C 112 for claims which encompass differentiating any type of thyroglobulin from any other type, including those yet undiscovered. The courts have held that:

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based In some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not In compliance with the first paragraph of U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill In the art; In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement In the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; In cases involving unpredictable factors, such as chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."In re Fisher 427 F.2d 833, 166 USPQ 18 (CCPA 1970)

Therefor one of skill in the art would not be enabled to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 U.S.C. § 103

4. Claims 49-66, 68-75, and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanham et al. Biochemica et Biophysica Acta, Vol 884, 1986, in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane Antibodies, a Laboratory Manuel, Chapter 14, pages 553-612, 1988 or Samuel et al., US Patent 5,242,799, September 7, 1993.

Hanham et al. teaches a method of measuring types of thyroglobulin and detecting malignancy in a fluid sample originating from a living body (a tissue sample which has been homogenized in PBS)(see methods, page 159) and the corresponding reagent. The method of Hanham et al. uses an anti-thyroglobulin antibody which is capable of binding to both types of thyroglobulin and further using a lectin (see for example "Lectin Affinity electrophoresis", page 160) which is capable of binding a specific sugar chain structure on only one of the two types of thyroglobulins. The method of Hanham et al. measures thyroglobulins using both antibodies and lectins in combination with one another. The methods include competitive binding assays and correlation of glycosylation variants (different types of thyroglobulins) to malignancy. (see pages 160-164, especially results and figures).

Although Hanham et al. does not necessarily specifically recite various order of steps or specific methods of measuring identical properties of the instant claims, those variations would be obvious to one of skill in the art, as routine art known variants of identical methods. For example, see Voller et al., or Harlow and Lane, both of which discuss the numerous assay methods encompassed by the instant claims. See also Samuel et al., US Patent 5,242,799, September 7, 1993, which discusses numerous lectin/antibody assays (columns 1-6). Further, it is obvious to alter the order in which steps of a known method are performed:

MPEP 2144.04 See In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Therefor it would have been prima facie obvious to one of ordinary skill in the art to modify the assay of Hanham et al. by varying the assay with art known assay techniques taught by Voller et al., or Harlow and Lane, or Samuel et al for the purpose of efficiency and convenience.

5. Claims 49-66, 68-75, and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Helig et al., Endocrinol. Suppl., 108(267), page 151, 1985, in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane Antibodies, a Laboratory Manuel, Chapter 14, pages 553-612, 1988 or Samuel et al., US Patent 5,242,799, September 7, 1993.

Helig et al. teaches a method of measuring types of thyroglobulin and detecting malignancy in a fluid sample originating from a living body and the corresponding reagent. The method of Helig et al. uses an anti-thyroglobulin antibody which is capable of binding to both types of thyroglobulin and further using an additional which is capable of binding a specific sugar chain structure on only one of the two types of thyroglobulins. The methods include competitive binding assays and correlation of variants (different types of thyroglobulins) to malignancy. (see entire document)

Although Helig et al. does not necessarily specifically recite various order of steps or specific methods of measuring identical properties of the instant claims, those variations would be obvious to one of skill in the art, as routine art known variants of identical methods. For example, see Voller et al., or Harlow and Lane, both of which discuss the numerous assay methods encompassed by the instant claims. See also Samuel et al., US Patent 5,242,799, September 7, 1993, which discusses numerous lectin/antibody assays (columns 1-6). Further, it is obvious to alter the order in which steps of a known method are performed:

MPEP 2144.04 See In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Therefor it would have been prima facie obvious to one of ordinary skill in the art to modify the assay of Helig et al. by varying the assay with art known assay techniques taught by Voller et al., or Harlow and Lane, or Samuel et al for the purpose of efficiency and convenience.

6. Claims 49-66, 68-75, and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al., Chung-hua Ping Li Hsueh Tsa Chin, Volume 19, No 2, pages 90-93, in view of Lancet, (1977). Vol. 1, No. 8017, pp. 881-882, and further in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane Antibodies, a Laboratory Manuel, Chapter 14, pages 553-612, 1988, or Samuel et al., US Patent 5,242,799, September 7, 1993.

Wang et al. teaches a method of measuring types of thyroglobulin and detecting malignancy in a tissue sample originating from a living body and the corresponding reagent. The method of Wang et al. uses an anti-thyroglobulin antibody which is capable of binding to both types of thyroglobulin and further using a lectin which is capable of binding a specific sugar chain structure on only one of the two types of thyroglobulins. The method of Wang et al. measures thyroglobulins using both antibodies and lectins in combination with one another. The methods include competitive binding assays and correlation of glycosylation variants (see abstract and full text translation)

Although Wang et al. teaches detection of thyroglobulin in tissues, the detection of thyroglobulin in serum and subsequent correlation to cancer is well known in the art (see for example Lo Gerfo et al., Lancet, (1977). Vol. 1, No. 8017, pp. 881-882)

Although Wang et al. does not necessarily specifically recite various order of steps or specific methods of measuring identical properties of the instant claims, those variations would be obvious to one of skill in the art, as routine art known variants of identical methods. For

example, see Voller et al., or Harlow and Lane, both of which discuss the numerous assay methods encompassed by the instant claims. See also Samuel et al., US Patent 5,242,799, September 7, 1993, which discusses numerous lectin/antibody assays (columns 1-6). Further, it is obvious to alter the order in which steps of a known method are performed:

MPEP 2144.04 See In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Therefor it would have been prima facie obvious to one of ordinary skill in the art to modify the assay of Wang et al. and Lo Gerfo et al., by varying the assay with art known assay techniques taught by Voller et al., or Harlow and Lane, or Samuel et al for the purpose of efficiency and convenience.

7. Claims 49, 50, 52, and 57-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Canfield et al., WO 87/00289, published January 15, 1987, in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane Antibodies, a Laboratory Manuel, Chapter 14, pages 553-612, 1988, or Samuel et al., US Patent 5,242,799, September 7, 1993.

WO 87/00289 teaches a method of measuring types of thyroglobulin in a fluid sample originating from a living body and the corresponding reagent. The method of WO 87/00289 uses an anti-thyroglobulin antibody which is capable of binding to both types of thyroglobulin and further using a lectin which is capable of binding a specific sugar chain structure on only one of

the two types of thyroglobulins. The method of WO 87/00289 measures thyroglobulins using both antibodies and lectins in combination with one another. The methods include competitive binding assays. (see especially pages 9-15)

Although WO 87/00289 does not necessarily specifically recite various order of steps or specific methods of measuring identical properties of the instant claims, those variations would be obvious to one of skill in the art, as routine art known variants of identical methods. For example, see Voller et al., or Harlow and Lane, both of which discuss the numerous assay methods encompassed by the instant claims. See also Samuel et al., US Patent 5,242,799, September 7, 1993, which discusses numerous lectin/antibody assays (columns 1-6). Further, it is obvious to alter the order in which steps of a known method are performed:

MPEP 2144.04 See In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Therefor it would have been prima facie obvious to one of ordinary skill in the art to modify the assay of WO 87/00289 by varying the assay with art known assay techniques taught by Voller et al., or Harlow and Lane, or Samuel et al for the purpose of efficiency and convenience.

8. Claims 49-66, 68-75, and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Canfield et al., WO 87/00289, published January 15, 1987, in view of Tarutani et al., Journal of Biochemistry, Volume 98, No. 3, 1985, or Wang et al., Chung-hua Ping Li Hsueh Tsa

Chin, Volume 19, No 2, pages 90-93, or Hanham et al. Biochemica et Biophysica Acta, Vol 884, 1986, or Helig et al., Endocrinol. Suppl., 108(267), page 151, 1985, and further in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane Antibodies, a Laboratory Manuel, Chapter 14, pages 553-612, 1988, or Samuel et al., US Patent 5,242,799, September 7, 1993.

WO 87/00289 teaches a method of measuring types of thyroglobulin in a fluid sample originating from a living body and the corresponding reagent. The method of WO 87/00289 uses an anti-thyroglobulin antibody which is capable of binding to both types of thyroglobulin and further using a lectin which is capable of binding a specific sugar chain structure on only one of the two types of thyroglobulins. The method of WO 87/00289 measures thyroglobulins using both antibodies and lectins in combination with one another. The methods include competitive binding assays. (see especially pages 9-15)

WO 87/00289 fails to specifically correlate sugar chain variants to cancer, however that variation in thyroglobulin sugar chains is indicative of cancer is well established in the art. See for example, Tarutani et al., or Wang et al., or Hanham et al., or Helig et al. (see for example, abstracts).

Further, although WO 87/00289 does not necessarily specifically recite various order of steps or specific methods of measuring identical properties of the instant claims, those variations would be obvious to one of skill in the art, as routine art known variants of identical methods. For example, see Voller et al., or Harlow and Lane, both of which discuss the numerous assay

methods encompassed by the instant claims. See also Samuel et al., US Patent 5,242,799, September 7, 1993, which discusses numerous lectin/antibody assays (columns 1-6). Further, it is obvious to alter the order in which steps of a known method are performed:

MPEP 2144.04 See In re Burhans, 154 F.2d 690, 69 USPQ 330 (CCPA 1946) (selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results); In re Gibson, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) (Selection of any order of mixing ingredients is prima facie obvious.).

Therefor it would have been prima facie obvious to one of ordinary skill in the art to modify the assay of WO 87/00289 by varying the assay to correlate to cancer, as taught by Tarutani et al., Wang et al., Hanham et al., or Helig et al. with art known assay techniques taught by Voller et al., or Harlow and Lane, or Samuel et al for the purpose of efficiency and convenience.

9. Claims 49-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Canfield et al., WO 87/00289, published January 15, 1987, in view of Tarutani et al., Journal of Biochemistry, Volume 98, No. 3, 1985, or Wang et al., Chung-hua Ping Li Hsueh Tsa Chin, Volume 19, No 2, pages 90-93, or Hanham et al. Biochemica et Biophysica Acta, Vol 884, 1986, or Helig et al., Endocrinol. Suppl., 108(267), page 151, 1985, and further in view of Voller et al. Rul. World Health Organ., Vol. 53, pages 55-65, 1976, or Harlow and Lane Antibodies, a Laboratory Manuel, Chapter 14, pages 553-612, 1988, or Samuel et al., US Patent 5,242,799 and further in view of Larena, et al., Langenbecks Archiv fur Chrurgie Vol 381/2 pages 102-113 1996.

WO 87/00289, and Tarutani et al., Wang et al., Hanham et al., or Helig et al., and Voller et al., or Harlow and Lane, or Samuel et al. teach as set forth above and applied to claims 49-66, 68-75, and 77 supra. WO 87/00289, and Tarutani et al., Wang et al., Hanham et al., or Helig et al., and Voller et al., or Harlow and Lane, or Samuel et al. fail to teach an anti-thyroglobulin antibody reactive with a Lewis type sugar chain.

Larena et al. teaches that Lewis type sugar chains are known in the art to be useful for detection of malignancy, including thyroid malignancy. Larena compares levels to total thyroglobulin to Lewis expressing thyroglobulin as well as normal thyroid tissue to cancerous tissue.

Therefor it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the antibody of Larena et al. as the anti-thyroglobulin antibody in the methods of any of WO 87/00289, and Tarutani et al., Wang et al., Hanham et al., or Helig et al., and Voller et al., or Harlow and Lane, or Samuel et al. because the antibody is detectable in normal and cancerous tissue and useful for determination of thyroid malignancy as set forth in Larena et al.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Hunt, whose telephone number is (703) 308-7548. The examiner can normally be reached Monday through Thursday 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (703) 308-3995. The fax number for the group is (703) 305-3014 or (703) 308-4242.

Communications via internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**anthony.caputa@uspto.gov**].

All internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists the possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist, whose telephone number is (703) 308-0196.

Jennifer Hunt

July 2, 2001

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600